UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

77974 7590 10/07/2008

Bozicevic, Field & Francis LLP
Stanford University Office of Technology Licensing
1900 University Avenue
Suite 200
East Palo Alto, CA 94303

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/07/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,322	10/14/2003	Gilbert Chu	STAN-277	7388

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR DETERMINING RISK OF TREATMENT TOXICITY

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$300	$0	$1055	01/07/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 08/07) Approved for use through 08/31/2010.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

77974 7590 10/07/2008

Bozicevic, Field & Francis LLP
Stanford University Office of Technology Licensing
1900 University Avenue
Suite 200
East Palo Alto, CA 94303

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,322	10/14/2003	Gilbert Chu	STAN-277	7388

TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR DETERMINING RISK OF TREATMENT TOXICITY

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	$755	$300	$0	$1055	01/07/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
CALAMITA, HEATHER	1637	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) the names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ❑ Individual ❑ Corporation or other private group entity ❑ Government

4a. The following fee(s) are submitted:

❑ Issue Fee

❑ Publication Fee (No small entity discount permitted)

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s): **(Please first reapply any previously paid issue fee shown above)**

❑ A check is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

❑ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

❑ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____ Date _____

Typed or printed name _____ Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,322	10/14/2003	Gilbert Chu	STAN-277	7388

77974 7590 10/07/2008

Bozicevic, Field & Francis LLP
Stanford University Office of Technology Licensing
1900 University Avenue
Suite 200
East Palo Alto, CA 94303

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 10/07/2008

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 355 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 355 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

Notice of Allowability	Application No.	Applicant(s)	
	10/686,322	CHU ET AL.	
	Examiner	Art Unit	
	HEATHER G. CALAMITA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the reply filed December 3, 2007*.

2. ☒ The allowed claim(s) is/are *17, 20, 21, 23, 26-30 and 47 and 51*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Heather G. Calamita, Ph.D./ Examiner, Art Unit 1637	/GARY BENZION/ Supervisory Patent Examiner, Art Unit 1637

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Pamela Sherwood on September 26, 2008.

The application has been amended as follows:

Cancel claims 22, 32, 33, 48 and 49.

IN THE CLAIMS:

17. A method of determining the suitability of a patient for radiation therapy, the method comprising:

predicting whether a subject will be susceptible to undesirable toxicity resulting from treatment with radiation therapy, said method comprising:

(a) obtaining transcriptional expression profile for the response to radiation for a sample from said subject from a set of sequences comprising:

Cyclin B, ATP synthase, CDC28, protein kinase 2, forming-binding protein 17, ribosomal protein 17, ribosomal protein S9, phorbolin-like protein MDS019, tumor necrosis factor superfamily member 7, RNA helicase disrupter of silencing 10, heat shock 27 kD protein 1

(b) comparing said obtained expression profile to a reference expression profile from a cell known to have a susceptible phenotype for radiation toxicity to determine the probability that said patient is susceptible to undesirable radiation toxicity;

wherein a patient that is predicted to have a high probability of undesirable radiation toxicity is less suitable for radiation therapy.

20. The method according to Claim 17, wherein said expression profile further comprises expression data from RAD23 homolog B, chromobox homlog 1, heterogeneous nuclear ribonucleoprotein A/B,

proteasome subnunit beta type 4, Bromodomain adjacent to zinc finger domain, ubiquitin, nudix-type motif 1, U6 snRNA-associated Sm-like protein, eukaryotic translation termination factor 1, poly(A)-binding protein cytoplasmic 1, U6 snRNA-associated Sm-like protein LSm7, calmodulin, interferon regulatory factor 4, solute carrier family 25 (mitochondrial carrier; adenine IR nucleotide translocator) member 6, serum response factor (c-fos serum response IR element-binding transcription factor), eukaryotic translation elongation factor 2, ATP synthase H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein), cyclin A2, maternal G10 transcript, proteasome (prosome, macropain) 26S subunit non-ATPase 1, muscle specific gene, DR1-associated protein 1 (negative cofactor 2 alpha) splicing factor proline/glutamine rich (polypyrimidine UV tract-binding protein-associated), Cyclin B1, aldo-keto reductase family 1member B1 (aldose IR reductase), mitogen-activated protein kinase-activated protein kinase 2, mitochondrial ribosomal protein L23, solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator) member 5, protein phosphatase 1A (formerly 2C) magnesium-dependent alpha isoform, alanyl-tRNA synthetase, ribosomal protein S11, transmembrane 7 superfamily member 2, KIAA0370 protein, KIAA1115 protein, proteasome (prosome, macropain) activator subunit 2 (PA28 beta), translocase of outer mitochondrial membrane 20, (yeast) homolog, RuvB (E coli homolog)-like 1, core-binding factor, beta subunit.

23. A method of optimizing radiation therapy for a patient, the method comprising:

(a) obtaining transcriptional expression profile for the response to radiation for a sample from said subject from a set of sequences comprising:

Cyclin B, ATP synthase, CDC28, protein kinase 2, forming-binding protein 17, ribosomal protein 17, ribosomal protein S9, phorbolin-like protein MDS019, tumor necrosis factor superfamily member 7, RNA helicase disrupter of silencing 10, heat shock 27 kD protein 1; and

(b) comparing said obtained expression profile to a reference expression profile from a cell known to have a susceptible phenotype for toxicity from the anti-proliferative therapy to determine the probability that said patient is susceptible to undesirable toxicity;

wherein a dose of said anti-proliferative therapy is selected to minimize to undesirable toxicity, while providing for effective anti-proliferative activity.

26. A method of obtaining an expression profile for the transcriptional response to radiation, the method comprising:

exposing a cell sample from an individual to radiation;

extracting mRNA from said cell;

quantitating the level of mRNA from a set of sequences comprising:

Cyclin B, ATP synthase, CDC28, protein kinase 2, forming-binding protein 17, ribosomal protein 17, ribosomal protein S9, phorbolin-like protein MDS019, tumor necrosis factor superfamily member 7, RNA helicase disrupter of silencing 10, heat shock 27 kD protein 1; and

comparing said level of mRNA to the level of said mRNA present in a cell sample from said individual not exposed to radiation, wherein said comparing step comprises a nearest shrunken centroid analysis step.

50. The method of Claim 23, wherein said expression profile further comprises expression data from from RAD23 homolog B, chromobox homlog 1, heterogeneous nuclear ribonucleoprotein A/B, proteasome subnunit beta type 4, Bromodomain adjacent to zinc finger domain, ubiquitin, nudix-type motif 1, U6 snRNA-associated Sm-like protein, eukaryotic translation termination factor 1, poly(A)-binding protein cytoplasmic 1, U6 snRNA-associated Sm-like protein LSm7, calmodulin, interferon regulatory factor 4, solute carrier family 25 (mitochondrial carrier; adenine IR nucleotide translocator) member 6, serum response factor (c-fos serum response IR element-binding transcription

factor), eukaryotic translation elongation factor 2, ATP synthase H+ transporting, mitochondrial F1 complex, O subunit (oligomycin sensitivity conferring protein), cyclin A2, maternal G10 transcript, proteasome (prosome, macropain) 26S subunit non-ATPase 1, muscle specific gene, DR1-associated protein 1 (negative cofactor 2 alpha) splicing factor proline/glutamine rich (polypyrimidine UV tract-binding protein-associated), Cyclin B1, aldo-keto reductase family 1member B1 (aldose IR reductase), mitogen-activated protein kinase-activated protein kinase 2, mitochondrial ribosomal protein L23, solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator) member 5, protein phosphatase 1A (formerly 2C) magnesium-dependent alpha isoform, alanyl-tRNA synthetase, ribosomal protein S11, transmembrane 7 superfamily member 2, KIAA0370 protein, KIAA1115 protein, proteasome (prosome, macropain) activator subunit 2 (PA28 beta), translocase of outer mitochondrial membrane 20, (yeast) homolog, RuvB (E coli homolog)-like 1, core-binding factor, beta subunit.

2. The following is an examiner's statement of reasons for allowance: The claims are drawn to a method of determining the suitability of a patient for radiation therapy by determining susceptibility of the patient to radiation toxicity using an expression profile of ten genes. The closest prior art is Komarova et al. (Oncogene, 1998). Komarova et al., however looks only at cyclin B. The instant claims require a profile of at least 10 specific genes. There is no teaching or suggestion in the prior art directing the skilled artisan to choose these specific genes. The claims are therefore unobvious over the prior art.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Correspondence

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on

Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637